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(54) Title: DAIRY PRODUCTS

(57) Abstract

Low homocysteinogenic dairy products enriched with Vitamin B6, and optionally folic acid, Vitamin B12, and magnesium. Dairy products containing specific proportions of methionine, cysteine, Vitamin B6, folic acid, Vitamin B12, and magnesium.

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DAIRY PRODUCTS

The present invention relates to low homocysteinogenic dairy products enriched with Vit B6 and optionally with folic acid, magnesium, cysteine and Vit B12.

Most of the scientific literature regarding to the significance of hyperhomocysteinemia relates to cardio-vascular-disease (CVD). However, it has been found that hyperhomocysteinemia is associated also with other health and mental risks, e.g. high homocysteine (HCY) and manic depressions, seizure disorders, depression, asthma and migraine headaches. All said diseases respond extremely well to Vit B6 therapy. (Braverman and Pfeiffer, 1987, In: The Healing nutrients within, D. Homocysteine, p. 155-162, Keats Pub-lish.Inc.New Canaan, Conn.). This can be done due to the fact that HCY is a most exicatory amino acid. Representative reports regarding recent research evidence on the mental implications of hyper-HCY and/or interrupted sulfur-amino acid metabolism are in particular presented in the following articles:

Regland et. al., J. Neural. Transmission general section, 1994, 98(2):143-152; Regland et. al., 1995 J. Neural Transmission, general section, 100(2):165-9; Santhosh et. al., 1995, Medical Hypothesis, 43(4):239-244).

HCY or tHCY in connection with the present invention refer to the sum of the multiple forms of homocysteine, homocystine and cysteine-homocysteine complex.

The significance of hyper-HCY for skeletal and cross linking of collagen was also documented in animal models and in humans. (Cook et. al., 1994, Poult. Sci. 73(6):889-96; Wolos

et. al., 1993, J. Immunol. 151(1):526-34; Levene et. al., 1992, Int. J. Exp.Pathol. 73(5):613-24; Masse et. al., 1990, Scanning. Microsc. 4(3):667-73 discussion on p.674).

The issue of the relationship of CVD and of hyper-HCY was recently recognized as a major dietary risk factor. (Stampfer et. al., 1992, JAMA, 268:877-881; Dywer, 1995,J. Nutr. 125 (3rd supplement): 656-665s). Levels of HCY associated with elevated risk of myocardial infarct (MI) are common among U.S. adults. (Willet, 1995, J. Nutr. 125 (3rd supplement): 647-655s). In the Framingham heart study 20% of the individuals had high plasma HCY which was associated with low intake of Vit B6 and of folic acid. (Selhub et. al., 1993, JAMA, 271:2193-8).

Many studies have shown that elevated total HCY levels are frequently found in patients suffering from arteriosclerosis effecting coronary, cerebral and peripheral arteries. (Clarke et. al., 1991, N. J. Med. 324:1149-1155); Bors et. al., 1995, N. Engl. J. Med. 818:709-715; Duduman et. al., 1993, Arterioscler. Tromb. 18:1253-1260; Stabler et. al., 1988, J. Clin. Invest. 81:466-1974; Malinow et. al., 1990, Coron. Arter. Dis., 1:215-20; Franken et. al., 1994, Arterioscl. Thromb., 14:465-70). Earlier studies had shown that the effect of HCY levels on vascular diseases appeared to be independent from LDL or HDL, diabetes mellitus, smoking body mass index, high blood pressure and age. (The LDL is the high cholesterol and high risk fraction in the human plasma. HDL is the protective lipoprotein fraction). (Pancarunity et. al., 1994, Am. J. Clin. Nutrit. 59:941-8)

The above considerations lead to the conclusion that hyperhomocysteinemia is an independent risk factor although some correlations exist between HCY with other risk factors, i.e. between HCY and advanced age, reduced physical activity, increased smoking, higher cholesterol levels and increased diastolic pressure. (Nygard et. al., 1995, JAMA, 274(19:1526-33).

A meta-analysis provided considerable evidence that elevated HCY levels were associated with an increased risk of arteriosclerotic vascular diseases. This association meets the criteria of causality (Ill AB, 1965, Proc. R. Soc. Med. 58:295-300), consistency, strength, temporality and biological plausibility. Elevated t-HCY levels precede the occurrence of coronary heart diseases. (Stampler et. al., 1992, JAMA268:877-881). Early signs of premature carotid arterial stenosis were found by ultrasound among heterozygoses for homocysteinuria. (Rubbet. al. 1990, Metabolism 1191-1195; Clarke et. al., 1992, Ir. J. Med. Sci. 161:61-65) and in individuals with moderate hyperhomocysteinemia. (Malinow et. al., 1993, Circulation, 87:332-328-329; Sehlhub et. al., 1995, N. Engl. J. Med. 332:286-291); Stampfer et. al., 1995, N. Engl. J. Med. 332:328-329). The association was consistent across studies by different investigators using a variety of methods in different populations of various geographic areas. Both prospective and case-controlled studies indicate a significant positive association. (Boushey et. al., 1995, JAMA, 274:1049-1057).

BIOLOGICAL MECHANISMS

For a long time the administration of HCY was used as an experimental tool to demonstrate that endothelial cell damage is probably an essential preliminary factor for the development of atherosclerotic plaques.

Direct toxicity of HCY to the endothelium has been reported in laboratory studies (Dudman et. al., 1993, Atherocler. Thromb., 13:1253-1260; Wall et. al., 1980, Thromb. Res. 18:113-121; Blann, 1994, Atherosclerosis, 94:89-91), but under much higher concentrations than have been found in vivo.(Harker et. al.1976, J. Clin. Invest. 58: 731-741; Mudd et. al., 1995, Disorders of trans-sulfuration. The metabolic and molecular bases of inherited disease, N.Y. McGraw-Hill Inc. 1279-1327) Fenton and Rosenberg, 1995, (Inherited disorders, of Cobalamine transport and metabolism in Scriver et. al., Eds, N.Y. McGraw Hill Inc. 3129-3149,) showed endothelial desquamation in vivo in baboons infused with HCY or homocystine at the high levels typical of patients with homocystinuria. HCY has also been shown to increase DNA synthesis in vascular smooth muscle cells being consistent with early arteriosclerotic lesions and to induce these cells to proliferate while impeding the regeneration of endothelial cells (Arker et. al., 1974, N. Engl. J. Med. 291:537-543), to disrupt cross linking and thus to inhibit cysteine and glutathione (Braverman et. al., 1987). Moreover, it causes oxidation of LDL (Heinecke et. al., 1984, J. Clin. Invest., 74:1890-1894), that leads them to be recognized by human arterial smooth muscle cells in culture (Parthasaraty, 1987, Biochim. Biophys. Acta, 917:337-350). The effects of HCY on

vascular hemostatic properties have included decreased thrombo modulin cell surface expression and inhibition of protein C activation, thus probably contributing to the development of thrombosis (Rosenblat et. al. Inherited disorders of folate transport and metabolism, 1995, N.Y. McGraw Hill Inc. 3111-3128).

GENETIC FACTORS

The variation in serum HCY in the population reflects both genetic and nutrition factors. Comparison of identical and non-identical twins have suggested a high heritability of high HCY levels (Berg et. al., 1992, Clin. Genet. 41:315-321; Reed et. al., 1991, Clin. Genet., 89:425-428). However, the presence of proband-spouse correlations indicate a role for nutritional factors. (Williams et. al., Dis. 1990, Coron. Arthery., 1:681-685; Genest et. al., 1991, Arterioscler. Thromb. 11:1129-1136).

A thermolabile variant of methylene tetrahydro folate reductase can explain about 17% of CVD patients and 28% of patients suffering of a premature vascular disease who had hyperhomocysteinemia. The latter condition can be treated by administering folic acid (Kang et. al., 1988, Am. Hum. Genet. 43:414-421).

Altogether the genetic origin of the high tHCY can most probably not account for the frequency of hyperhomocysteinemia in the population.

NUTRITIONAL FACTORS

Besides the genetic factors, which in most cases are successfully handled by dietary supplements, hyperhomocysteinemia may result primarily from diet due to

either high intake of methionine or inadequate intake of the cofactors Vit B6, folic acid, magnesium, cysteine and/or Vit B12 which are involved in converting HCY into methionine or degradation of HCY to keto-butyrate. Both conditions, namely high methionine and low Vit B6 and/or other cofactors can exist in animal protein, i.e. in dairy products.

*THE RISK OF HIGH METHIONINE DIETS:

Feeding rabbits a methionine enriched diet for 6-9 months resulted in a significant increase in plasma and in aortic TBARS levels and in aortic antioxidative enzyme activities. Histological examination of aortas showed typical atherosclerotic changes, e.g. blood vessles' intimal thickening, deposition of cholesterol and calcification (Toborek et. al. 1995, Atherosclerosis, 115(2):217-24).

In mini pigs, high methionine, caseinate based diet lead to hyperhomocysteinemia which induced vascular alterations favoring the viscous component vs the elastic component (Roland et. al., 1995, Circulation, 91(4):1161-74.) Tumor cells are totally dependent on exogenous methionine whereas normal cells may substitute for an alternative sulfur compound. This difference was suggested to be used for a therapeutic purpose (Breillout et. al., 1990, J. Nat. Cancer. Inst., 82(20):1628-32).

THE ANTI-RISK CO-FACTORS

VIT B6:

Homocysteine is a natural amino acid metabolite of the methionine, but it occurs only transiently before being converted into the harmless cystathionine by (Cystathionine synthase). Cystathionine is then cleaved to form cysteine, 2-ketobutyrate and ammonium ions (by cystathioninase). Both enzymes involved comprise pyridoxal (Vit B6) phosphate as coenzyme.

It has long been known that low Vit B6 intake may produce arterial intimal damage. McCully et., al., 1975, (Artheriosclerosis, 22:215-227) noted that children with homocysteinuria, characterized by homozygous deficiency of cystathionine synthase, suffer early in life from atherosclerosis. The authors hypothesized that even less extreme levels of homocysteinemia may increase coronary heart disease risk prematurely.

It has been found that addition of Vit B6 (pyridoxine) is the most effective additive in reducing elevated HCY following a methionine load test, whereas folic acid has been found to be most effective in reducing fasting HCY (Brattstrom et. al., 1990, Atherosclerosis, 81:51-60; Brattstrom et. al., 1992, A. Neural. Res., 14:81). The addition of Vit B6 did not prevent high fasting plasma HCY in adults but it reduced the HCY levels in fast growing rats when the requirements of HCY were increased (Coburn, 1990, Ann. N.Y. Acad. Sci., 585:76-85) as well as under methionine load (Miller et. al.,1992, Am. J.

Clin. Nutr. 55:1154-1160). Hyperhomo- cysteinemiacysteinemia was defined by two alternative measures, namely high fasting level and/or after oral methionine loading. Bother showed to be independent risk factors for CVD (Bostom et. al., Artherosclerosis, 116:147-51). The authors found that 75% of those with post-methionine loading hperHCY had fasting total HCY concentrations below the 75th percentile (10.7 mcmole/1). They therefore concluded that fasting total plasma HCY determination alone fails to identify a sizable percentage, more than 40% of persons who have clinically relevant hyperhomocysteinemia post methionine loading. This emphasizes the importance of Vit B6 coming together with high methionine foods. Folic acid can reduce HCY by re-mythlation and thus produce methionine. Thus this step seems to be less effective under methionine load.

Vit B6 deficiency can block the pathway of HCY catabolism to cysteine and thus reduce the availability of cysteine. Accumulated aggregates of HCY with cysteine to form mixed disulfides can further lead to secondary cysteine deficiency, that can effect the glutathione antioxidative system, which is important for cardio-vascular health. Diets high in meat and dairy products, which comprise a large amount of methionine, require more Vit. B6, but often cont .n less B6 due to losses during food processing (Papaioannou, 1986, Medical Hypothesis, cited in Braverman and Pfeiffer al., 1987). Supplementing Vit B6 to rats, following 5 weeks on a Vit B6 deficient diet based on 70% casein dramatically decreased the liver ratio methionine:HCY which causes the reduction of the ratio PE

(phosphatidyl ethanol) to PC (phosphatidyl-choline) in liver microsomes (She et. al., 1995, Biosci. Biotechnol. Biochem., 59(2): 163-7).

Folic Acid:

Homocysteine increases as folic acid decreases in plasma of healthy men during short term dietary folic acid and methyl group restriction (Jacob et. al., J. Nutr. 1994, 124(7):1072-80). The possible association of folic acid deficiency with homocysteinemia was recently investigated. (Kang et. al., 1987, Metabolism 36; 458-462; Stabler, et. al., 1988, J. Clin. Invest. 81:466-74). They demonstrated a striking negative correlation between serum folic acid concentrations and protein-bound HCY. Moderate to severe homocysteinemia was observed in all subjects with serum folic acid concentrations of 4.5 nmol/1 and in the majority of subjects with low normal serum concentrations (4.5-8.8 nmol/1). HCY concentrations ranging from 17-185 mcmole/1 (normal 7-22) were observed in 18 of 19 folic acid deficient individuals. These findings provide a new biochemical test for the assessment of the folic acid nutritional status. The homocysteinemia was corrected by the oral addition of folic acid (1 mg/d) but reappeared 12 weeks after said addition was discontinued. Kang et. al.; 1988 (Metabolism 37:611-613) surprisingly found that a high proportion (20%) of coronary heart disease patients suffered from thermolabile methylene tetrahydro folic acid reductase. As a result of the half-life of the body folic acid seems to be shorter than normal as indicated by the rapid reappearance of

homocysteinemia after discontinuation of the addition of folic acid. Thus, it seems that the homocysteine metabolism is dependent also on the presence of a suitable amount of vit B12, folic acid and under certain circumstances of betaine.

These results support previous suggestions that increased plasma homocysteine concentrations provide a marker of functional folic acid deficiency and further indicate that individuals may differ greatly in their susceptibility to hyperhomocysteinemia due to low folate intakes.

Folic acid appears to be the most effective agent against hyperHCY as it reduced fasting levels even when given alone. Low folic acid status is most commonly caused by low dietary folic intake (Stampfer, et. al., 1995, N. Eng. J. Med., 332:328-329).

400 mcg of folic acid/day is required to level plasma HCY (Davis et. al., 1994, Faseb. J. 8:A248 Abstract). This requirement resulted in the public health proposal for folic acid fortification, i. e., addition to flour and grains at 350 mcg/100 g (Boushhey, et. al., 1995, JAMA, 274:1049-1057).

The folic acid-Vit B12 required re-methylation of homocysteine to methionine normally converts ~50% of available homocysteine back to methionine. When this step is inhibited, either due to Vit B12 deficiency or inborn faults of Vit 12 metabolism or folic acid metabolism, it was shown to elevate the concentration of circulating homocysteine to values thought to represent an important risk factor for the development of occlusive vascular disease (Baum-gartner, et. al., 1980, J.

Inherited Metab. Dis.:101-103; Kang, et. al., 1986, U. Clin. Invest 77:1482-1486.)

VIT B12:

Vit B12 alone is effective in lowering HCY levels in cases with overt cobalamine deficiency (Brattstrom et. al., 1990, Atherosclerosis, 81:51-60; Brattstrom et. al., 1988, Metabolism, 37:175-178; Lindenbaum et. al., 1988, N. Eng. J. Med. 818:1720-1729).

The close association between Vit B12 and HCY suggests that HCY is another indicator of intracellular cobalamine functions in adults and in youngsters (Schneede et. al., 1994, Pediatr. Res. 36(2):194-201). Vit B12 deficiency in sheep caused lipid accumulation, peroxidation and decreased liver Vit E (Kennedy et. al. 1994, Int. J. Vitam. Nutr. Res., 64(4):270-6). This results suggest that the initiation of peroxidation is related to the increase in plasma homocysteine.

MAGNESIUM:

Recently it was found that magnesium is essential for the Vit B6 function as the enzyme pyridoxal phosphatase is activated by magnesium and inhibited by calcium (Fonda et. al. 1995, Arch. Biochem. Biophys. 320(2):345-52). The formation of S-adenosyl-
methionine (SAM), via the methionine adenosyl transferase enzyme, which is the first step in the methionine metabolism, is dependent on the presence of an appropriate amount of

magnesium. The SAM is formed by the transfer of the adenosyl group from adenosyl-triphosphate (ATP) to the sulfur atom of methionine. Recently it was suggested that SAM activates the cystathionine - ß-synthase even under
Vit B6 deficiency. This emphasizes the importance of the presence of magnesium in the high methionine metabolic environment (Miller et. al. 1992, Am. J.Clin. Nutr., 55:1154-1160). Milk products comprise generally a low amount of magnesium and the ratio methionine/magnesium is very high. Enriching the milk product with magnesium could contribute to facilitate the methionine metabolism.

THE TECHNOLOGICAL FOOD ENVIRONMENT

DAIRY PRODUCTS:

Dairy products are among the foods highest in methionine/VIT B6 ratio in low fat Ricotta, for example, the ratio methionine/ Vit B6 is 14245:1 (mg/mg). In many beef varieties it is around 2000 and in many cereals it is around 500. Regarding the RDA (recom- mended daily allowance) 1 cup (226 g) of low fat cottage cheese 2% contains 934 mg of methionine, which corresponds about to 200% of the RDA but only 0.172 mg of Vit B6 which is 8.6% of the RDA. In this case the ratio methionine:Vit B6 is 5430. At the same time, the concentrations of folic acid and magnesium are proportionally quite low, i.e. one cup of low fat 2% cottage cheese contains 16% and 4% of the RDA for folic acid and magnesium, respectively. Here, the methionine concentration (as % of RDA) is 20, 13, and 50 times higher than that of the above metabolic cofactors,respectively.

CASEIN:

Research studies showed that the presence of casein rendered the diet much more atherogenic and cholesterolemic than soy protein or flour (Howard et. al., 1965, Atherosclerosis Res. J. :330-337). Plasma cholesterol concentrations was doubled in rabbits fed on casein based cholesterol free diets 3.23 mmol/1 compared to 1.37 and 1.66 following soy protein and basal diets, respectively. (Meeker et. al. 1940, 1941, cited in Kritchevsky, 1995, J. Nutr. 125:589S-593S.) The authors attributed the difference to the amino acid composition of the individual proteins. Kritchevsky et. al. 1959, Arch. Biochem. Biophys., 85:444-451)) examined the effects of casein and of soy protein in conventional and germ free chickens. The casein-containing diet was more cholesterolemia in every case.

WHEY

Compared with the casein fraction in milk, in Whey-Acid-Dry the proportions of the cofactors are much better: in 100 g of whey (345Kc) of 49% RDA of methionine and 39, 19, 124 and 74% of RDA for Vit B6, folic acid, Vit B12 and magnesium, respectively.

Human milk has a much higher whey : casein ratio than cows milk. Increasing the ratio of the Whey fraction is the basic step for converting cows milk ingredients into humanized infant milk formula.

Low amounts of cysteine are part of the risks related to improper methionine and homocysteine metabolism and/or hyperhomocysteinemia.

Human milk as other initial foods, e.g. eggs and wheat germ, comprises a high proportion of cystine, i.e. the ratio methionine: cystine for wheat germ is 1.0 and for eggs 1.3. Compared to 3.3 in low fat, 2% cottage cheese; 2.4 for cream cheese (35% fat); and 3.2 for low fat yoghurt.

DEFICIENCIES RELATED TO PROCESSING

Vit B6:

Vit B6 is water-soluble. It is very sensitive. Processing can result in considerable loss of its activity: 15 to 70% in freezing fruits and vegetables; 50% to 70% in processing meats, 50% to 90% in milling grain.

FOLIC ACID:

Folic acid is water soluble, is easily destroyed by cooking, and is susceptible to degradation by processing and canning of vegetables and refining of grains.

Vit B12:

Vit B12 is relatively stable in heat and light. It is stored to some degree in liver, kidney, lungs and spleen. Thus, it can be balanced easier, and not all the required amount has to be eaten every day.

CYSTEINE:

A further advantage of human milk resides in the fact that it comprises a larger amount of cysteine. Whereas in human milk the ratio of methionine to cystine is 1:1, in cows milk it is 3:1. Cysteine, is a very crucial amino acid involved in the production of glutathione, which is a main factor in the detoxification and antioxidative systems. Glutathione, a cysteine-containing tripeptide, is the most abundant non-

protein thiol in mammal cells. Glutathione plays an important role in the detoxification of xenobiotic compounds and in the antioxidation of reactive oxygen species and free radicals. Its major function and involvement in diseases explain how dietary changes for increasing its concentration is important (Bray et. al., 1993, Can J. Physiol. Pharmacol. 71(9): 746-51). The supply of glutathione for detoxification purposes may be reduced by the supply of intracellular cysteine to serve as a precursor for glutathione synthesis through the gamma glutamyl cycle (Smith et. al., 1991, Adv. Exp. Med. Biol. 289:165-9.

When sulfur amino acids effects on blood lipids were compared in rats, serum lipid values were greater on proteins supplemented with methionine, while the addition of cysteine produced lower lipid levels (Kis, 1990, Plant Foods Hum. Nutr. 1990 40(4):297-308). A recent research showed that animal proteins, such as casein, are more hypercholesterolemic than soy protein, interpreted as mainly due to the presence of lysine and methionine. The effect was more pronounced in hypercholesterolemics (Carrol et. al., 1995, J. Nutr. 125 (3 supplement): 594S-597S)

It has thus been desirable to produce dairy products in which the amounts of the cofactors of the methionine metabolism, in particular of Vit B6, and optionally of magnesium, folic acid, Vit B12, and cysteine are increased.

The present invention thus consists in a dairy product in which the ratio methionine:Vit B6 (mg/mg) is 100 - 1400 : 1, preferably 300 - 600 : 1, advantageously 340 - 400 : 1.

Said ratio may also be calculated on the basis of methionine/protein : Vit B6 (the term methionine/protein (met/prot) defines how much methionine is part of the protein present) as follows:0.017-0.024(methionine/protein)340-550 : 1 (methionine/vit B6) 0.024-0.027: " 450-550 : 1 "

0.027-0.030: " 550-950 : 1 "

The ratio may also be calculated on the basis of the RDA. Thus, if the methionine contributes 200% of the RDA in order to attain 25% of the methionine the Vit B6 will increase to 50% of its own RDA. The preferred range is between 35-60% RDA of Vit B6/RDA of methionine.

The present invention also consists in dairy products which in addition to an increased amount of Vit B6 comprise increased compounds of one or more of the following cofactors:

Folic acid, magnesium, cysteine and/or Vit B12.

The ratio methionine : folic (mg/mg) acid should be 3000 - 8500: 1. It is preferably 3000 - 6500 :1,advantageously 3500-5000: 1.

The recommended ratios are, according to the concentration of the methionine in the protein:

0.017 - 0.024 3000 - 4000 : 1

0.024 - 0.027 3300 - 6500 : 1

0.027 - 0.030 6500 - 8000 : 1.

The ratio methionine : magnesium (mg/mg) should be 1.0 - 7.4 : 1, preferably 1.5 - 5.5 : 1 advantageously 2.0 - 3.7 : 1.

The recommended ratios are, according to the concentration of methionine in the protein:

0.017 - 0.024 1.0 - 2.0 : 1

0.024 - 0.030 2.0 - 3.0 : 1

0.027 - 0.030 3.0 - 7.0 : 1.

The ratio methionine : cysteine(mg/mg)should be0.5-5.5:1 preferably 1.5 - 3.8 : 1, advantageously 2.0 - 2.8. : 1.

The recommended ratios are, according to the concentration of the methionine in the product:

0.017 - 0.024 1.0 - 2.7 : 1

0.024 - 0.027 2.7 - 3.0 : 1

0.027-0.030 3.0 - 4.5 : 1.

The ratio methionine :Vit B12(mg/mcg)should be77 -600 : 1, preferably 100 - 470 : 1, advantageously 120 - 280 : 1.

As the ratio of methionine : Vit B12 is more dependent on the fermentation and on the bacteria activity it is not related to the concentrations of the protein nor to the methionine:protein ratio.

The present invention will now be illustrated with reference to the following examples without being limited by them. The examples present the suggested concentrations of Vitamins B6 and B12, folic acid, magnesium and cysteine. The marked figures represent firstly the original/endogenic concentration and then a final representative concentration.

The amounts to be added are complementary to the original concentrations. Thus, the added amount will be calculated by subtraction of the original content from the final desired

value. The percentages represent the values as % of the Israeli RDA for adult males (50-70).

When designing a Vit B6 enriched dairy product when the methionine analysis is not clear, the calculation will be performed in such a manner that the values are added for each ingredient.

EXAMPLES

ORIGINAL CONCENTRATION	FINAL CONCENTRATIONS	
Example 1		
CHEESE COTTAGE LOWFAT-1% - 1/2 CUP 113G.		
KCAL-82KC -4%		
PROTEIN- 14G -28%		
CARBOHYDRATE- 3G-1%		
FAT- 1.1G -2%		
Vit B6- 0,077MG-3.85%	0.54 MG	27%
FOLIC ACID-0.014MG-7%	0.047 MG	23%
Vit B12- 0.72MCG-36%		
CALCIUM- 69MG-9%		
MAGNESIUM- 6MG-1.7%	80 MG	23%
METHIONINE- 422MG-79%		
CYSTINE- 130MG-24%		
Example 2		
MILK 1% LOW-FAT-FLUID 1 CUP 244G		
KCAL- 102KC-5%		
PROTEIN- 8G-16%		
CARBOHYDRATE- 11.7G-4%		
FAT- 2.6G-7%		
Vit B6- 0.105MG-5.3%	0.36 MG	18%

FOLIC ACID -0.012MG-6%	0.056 MG	28%
Vit B12- 0.9MG-45%		
CALCIUM- 300MG-37%		
MAGNESIUM- 34MG-9.7%	87.5 MG	25%
METHIONINE- 201MG-38%		
CYSTINE- 74MG-14%		

Example 3

CHEESE-CREAM 1 OUNCE 28.35G

KCAL- 99.8KC-5%		
PROTEIN- 2.17G-4%		
CARBOHYDRATE- 0.8G-0%		
FAT- 9.98G-14%		
Vit B6- 0.013MG-0.65%	0.06MG	3%
FOLIC ACID- 0.004MG-2%	0.006MG	3%
Vit B12- 0.12MCG-6%		
CALCIUM- 23.26MG-3%		
MAGNESIUM- 2.0MG-0.6%	14 MG	4%
METHIONINE- 51.5MG-9.7%		
CYSTINE- 19.2MG-3.5%		

Example 4

MILK CHOCOLATE-1% LOWFAT 1 CUP 250G

KCAL- 158KC-7%		
PROTEIN- 8.1G-16%		
CARBOHYDRATE- 26G-9%		
FAT- 2.5G-3%		
Vit B6- 0.1MG-5%	0.36 MG	18%
FOLIC ACID- 0.012MG-6%	0.046 MG	23%
Vit B12- 0.855MCG-43%		

CALCIUM- 287MG-36%		
MAGNESIUM- 33MG-9.4%	98 MG	28%
METHIONINE- 203MG-38%		
CYSTINE- 75MG-14%		

Example 5

YOGURT-PLAIN-LOWFAT 1 CUP 227G

KCAL- 144KC-7%		
PROTEIN- 11.9G-24%		
CARBOHYDRATE- 16G-6%		
FAT- 3.6G-5%		
Vit B6- 0.11MG-5.5%	0.036 MG	18%
FOLIC ACID- 0.025MG-12.5%	0.050 MG	25%
Vit B12- 1.28MCG-64%		
CALCIUM- 415MG-52%		
MAGNESIUM- 40MG-11.4%	88 MG	25%
METHIONINE- 351MG-65%		
CYSTINE- 109MG-20%		

Example 6

CHEESE-COTTAGE WITH FRUIT 1/4 CUP 56G

KCAL- 69.8KC-3%		
PROTEIN- 5.6G-11%		
CARBOHYDRATE- 7.5G-3%		
FAT- 1.9G-3%		
Vit B6- 0.03MG-1.5%	0.36 MG	18%
FOLIC ACID- 0.0055MG-2.75%	0.046 MG	23%
Vit B12-0.28 MCG-14%	0.36 MCG	18%
CALCIUM- 27MG-3%		
MAGNESIUM- 2.25MG-0.6%	87.5 MG	25%

METHIONINE- 168MG-31%

CYSTINE- 51.8-9.7%

Example 7

CREAM - SOUR-CULTURED 1 CUP 230G

CKAL- 493KC-22%

PROTEIN- 7.27G-15%

CARBOHYDRATE- 9.8G-4%

FAT- 48G-66%

Vit. B6- 0.037MG-1.9%	0.46 MG	18%
FOLIC ACID- 0.025MG-12.5%	0.44 MG	22%

Vit B12- 0.69MCG-35%

CALCIUM- 268MG-33%

MAGNESIUM- 26MG-7.4%	87.5 MG	25%

METHIONINE- 184MG-34%

CYSTINE- 66.7MG-12%

Example 8

CHEESE-AMERICAN-PROCESSED

CKAL- 106KC-5%

PROTEIN- 6.27G-13%

CARBOHYDRATE- 0.45G-0%

FAT- 8.8G-12%

Vit B6- 0.02MG-1%	0.44 MG	22%
FOLIC ACID- 0.002MG-1%	0.050 MG	25%
Vit B12- 0.2MCG-10%	0.50 MCG	25%

CALCIUM- 174MG-22%

MAGNESIUM- 6MG-2%	77 MG	22%

METHIONINE- 162MG-30%

CYSTINE- 40MG-7%

Example 9

MILK CHOCOLATE WHOLE 1 CUP 250 G

KCAL- 208-9%

PROTEIN- 7.9G-14%

CARBOHYDRATE- 25.9GG-?%

FAT- 48G-12%

Vit B6- 0.1MG-5% 0.5MG 25%

FOLIC ACID- 0.012MG-6%

Vit B12- 0.835MG-42%

CALCIUM- 280MG-35%

MAGNESIUM- 33MG-9.4%

METHIONINE- 199MG-37%

CYSTINE- 73MG-13.6%

Example 10

YOGURT-PLAIN-WHOLE 1 CUP 227 G

KCAL- 139KC-6%

PROTEIN- 7.88G-16%

CARBOHYDRATE- 10.6g-4%

FAT- 7.38g-10%

Vit B6- 0.073MG-3.65% 0.036MG 18%

FOLIC ACID- 0.017MG-8.5%

Vit B12_ 0.844MCG-42%

CALCIUM- 274MG-34%

MAGNESIUM- 26MG-9%

METHIONINE- 232MG-43%

CYSTINE- 72.6MG-13.5%

Example 11

CHEESE RICOTTA SKIM MILK 1 CUP 246G

KCAL- 340KC-5%

PROTEIN- 28.G-56%

CARBOHYDRATE- 12G-5%

FAT- 19.6G-27%

6- 0.049MG-2.5% 2.0MG

100%

FOLIC ACID- 0.032MG-16%

Vit B12- 0.716MCG-36%

CALCIUM- 669MG-84%

MAGNESIUM- 36MG-10%

METHIONINE- 698MG-130%

CYSTINE- 246MG-46%

Claims

1. Dairy products in which the ratio methionine : Vit B6 (mg/mg) is 100 - 1400 : 1.

2. Dairy products according to Claim 1, wherein said ratio is 300 - 600 : 1.

3. Dairy products according to Claim 2. wherein said ratio is 340 - 400 : 1.

4. Dairy products according to any of Claims 1 to 3, which comprises also folic acid, wherein the ratio methionine : folic acid (mg/mg) is 3000 - 8500 : 1.

5. Dairy products according to Claim 4, wherein said ratio is 3000 - 6500 : 1.

6. Dairy products according to Claim 5. wherein said ratio is 3500 - 5000 : 1.

7. Dairy products according to any of Claims 1 to 6, which comprises also magnesium, wherein the ratio methionine : magnesium (mg/mg) is 1.0 - 7.4 : 1.

8. Dairy products according to Claim 7, wherein said ratio is 1.5 - 5.5 : 1.

9. Dairy products according to Claim 8, wherein said ratio is 2.0 - 3.7 : 1.

10. Dairy products according to any of Claims 1 to 9, which comprises also cysteine, wherein the ratio methionine : cysteine (mg/mg) is 0.5 - 5.5 : 1.

11. Dairy products according to Claim 10, wherein said ratio is 1.5 - 3.8 : 1.

12. Dairy products according to Claim 11, wherein said ratio is 2.0 - 2.8 : 1

13. Dairy products according to any of Claims 1 to 12, which comprises also Vit B12, wherein the ratio methionine : Vit B12 (mg/mcg) is 77 - 600 : 1.

14. Dairy products according to Claim 13, wherein said ratio is 100 - 470 : 1.

15. Dairy products according to Claim 14, wherein said ratio is 120 - 280 : 1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL97/00080

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A23C 9/00
US CL :426/580

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 426/072, 074, 580, 581, 582, 583, 584, 585, 586, 587, 588

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,871,550 A (MILLMAN) 03 October 1989, entire document.	1-6
Y	US 5,451,412 A (BOUNOUS ET AL) 19 September 1995, entire document.	1-6

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

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"P" document published prior to the international filing date but later than the priority date claimed

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19 JUNE 1997	25 JUL 1997
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer LESLIE WONG Telephone No. (703) 308-1979

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